Dissertation On

ANALYSIS OF ACUTE RENAL FAILURE IN POISON CONTROL AND TOXICOLOGY TRAINING CENTRE

submitted in partial fulfilment of requirements for

M.D. DEGREE BRANCH I GENERAL MEDICINE

of

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY, CHENNAI

MADRAS MEDICAL COLLEGE &

GOVT. GENERAL HOSPITAL

CHENNAI – 600 003.

MARCH 2008

CERTIFICATE

This is to certify that this dissertation entitled **"ANALYSIS OF ACUTE RENAL FAILURE IN POISON CONTROL AND TOXICOLOGY TRAINING CENTRE"** submitted by **Dr. R. SAKTHIRAJAN,** appearing for Part II M.D. Branch I General Medicine Degree examination in March 2008 is a bona fide record of work done by him under my direct audience and supervision in partial fulfillment of regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr.M.G.R. Medical University, Chennai, Tamil Nadu, India.

Director,
Institute of Internal Medicine,
Government General Hospital,
Chennai – 600 003.

Dean,
Madras Medical College,
Government General Hospital,
Chennai – 600 003.

DECLARATION

I solemnly declare that the dissertation titled **"ANALYSIS OF ACUTE RENAL FAILURE IN POISON CONTROL AND TOXICOLOGY TRAINING CENTRE"** is done by me at Madras Medical College & Govt. General Hospital, Chennai during 2005-2008 under the guidance and supervision of **Prof. P. THIRUMALAIKOLUNDU SUBRAMANIAN, M.D.**

The dissertation is submitted to The Tamilnadu **Dr.M.G.R.Medical University** towards the partial fulfillment of requirements for the award of M.D. Degree (Branch I) in General Medicine.

Place:

Date:

Dr. R. Sakthirajan
M.D. General Medicine
Postgraduate Student
Institute of Internal Medicine
Madras Medical College

ACKNOWLEDGEMENT

I would like to thank our Dean, **Dr.T. P. Kalaniti, M.D.,** who gave me permission to do this study in our institution.

I would like to express my sincere gratitude to our Professor and Director, Institute of Internal Medicine, **Prof.Thirumalaikolundu Subramanian, M.D.,** for his guidance and encouragement. With extreme gratitude, I express my indebtedness to him for his motivation, advice and valuable criticism, which enabled me to complete this work.

I also thank our Additional Professor **Dr. C. Rajendran, M.D.,** Chief of IMCU and Toxicology who permitted me to utilise the clinical resources of the unit and guided me throughout my study period through his advice and positive criticism.

I am extremely thankful to Assistant Professors of Medicine **Dr.R.Penchalaiah, M.D., Dr.K.V.S.Latha, M.D., Dr.Saravanababu, M.D.,** and **Dr. Vijayaraghavan,**

M.D., and the Assistant Professors of IMCU and Toxicology for their guidance and co-operation.

I would always remember with extreme sense of thankfulness for the co-operation and criticism shown by my Postgraduate colleagues.

I am immensely grateful to the generosity shown by the patients who participated in this study. If at all, this study could contribute a little to relieve them from their suffering I feel that I have repaid a part of my debt.

CONTENTS

INTRODUCTION

Acute renal failure (ARF) constitute 1.5% of all General Hospital admission in India (Jha *et al.,* 1992)[25]. Of which, 60% are due to medical causes. Among the medical causes diarrheal diseases, copper sulphate poisoning, snake bite & insect stings –together constitute 40% of causes (Chugh *et al.,* 1989) [15].

Compared to western countries, median age for ARF is relatively younger in tropical countries and is about 34 years (Chugh *et al.,* 1989)[15]. By affecting the productive age group, the toxic nephropathies have serious economic implication on the family as well as the community. Further, poverty, lack of medical facilities, lax legislation, ignorance, wide spread beliefs in indigenous system of medicine in rural areas leads to late presentation and multiorgan dysfunction, and the patients are pushed to a state of renal replacement therapy. All of them contribute to higher mortality than in developed countries.

By studying the etiologies, clinical pattern, the time delay in getting appropriate treatment and analysing outcome of toxic nephropathies, health care providers will be able to make a multi level approach to reduce its morbidity and mortality.

Aim of the Study

AIM OF THE STUDY

1. To find out the prevalence of acute renal failure among cases of acute poisoning,

2. To identify the underlying causes,

3. To assess the clinical pattern,

4. To elicit the predisposing factors and

5. To analyse the outcome.

Review of Literature

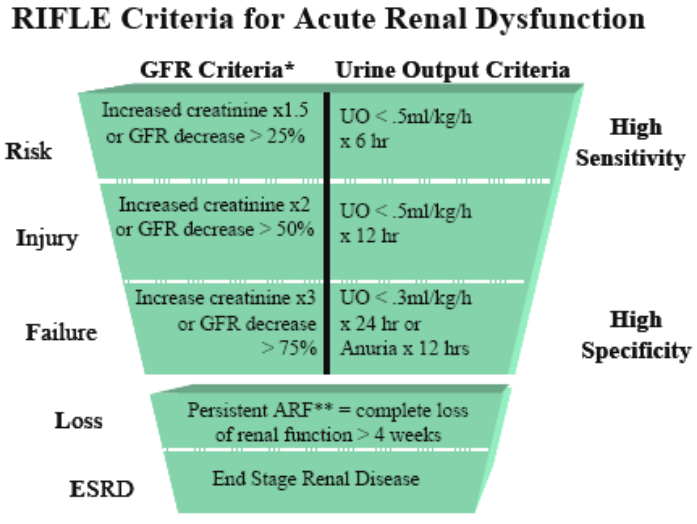
REVIEW OF LITERATURE

ACUTE RENAL FAILURE DUE TO POISONING

DEFINITION

Acute renal failure (ARF) is sudden decrease in the glomerular filtration rate (GFR) occurring over a period of hours to days and resulting in the failure of kidney to excrete nitrogenous waste products and maintain fluid and electrolyte homeostasis.

Practically and in clinical trials ARF is defined as per the RIFLE Criteria given below:



(Source : Results of the second Acute Dialysis Quality Initiative consensus conference (May 2002).

Epidemiology

The true incidence of toxic ARF in the tropics remain uncertain because of non specific nature of structural and functional abnormalities.

A good history is essential for the diagnosis, and requires questions about exposure to prescription and non-prescription drugs, herbal remedies, Industrial chemicals, fertilizers, paints, alcohol, etc., Traditional medicines containing nephrotoxins are encountered in developing countries. In many tribal populations, these medicines are obtained from a traditional healer or a witch – doctor. The indication for taking such medicines range from the frivolous like constipation, impotence and menstrual disorders to serious diseases such as cancer. Poisoning by traditional medicines in an important cause of death in many African countries. About 25 to 35 percent of all medical ARF in African Hospitals develops following ingestion of herbal medicines (Joubert and Sebata, 1982) [26]. In India true incidence of ARF due to

chemicals and herbal medicines is not available. Even in case of snake bite, information on the precise incidence of ARF in different geographical regions is lacking. The reported incidence from other countries varies between 1 and 27%. The incidence following Sawscaled viper or Russell's viper bite in India varies from 13 to 32% (Chugh *et al.,* 1984)[13].

ETIOLOGY RELATED TO POISONING

Classified into

Animal Poisons

a) Snake bite – Russell's Viper, Saw Scaled Viper, etc.

b) Spider bite

c) Bee, Wasp & Hornet Stings

d) Scorpion sting

e) Raw carp bile

Plant Poisons

a) Callilepis laureola poisoning

b) Djenkol bean

c) Mushroom Poisoning

d) Semecarpus anacardium

Chemicals

a) Copper sulphate

b) Ethylene glycol

c) Ethylene dibromide

d) Chromic acid

e) Lead

f) Cadmium

g) Mercury

h) Hydrocarbons

PATHOPHYSIOLOGY

Nephrotoxic substances may cause injury at a number of sites along the nephron and produce characteristic clinical syndrome. The following mechanisms are responsible for renal dysfunction in toxic nephropathies.

a) Proximal tubular injury

b) Renal Medullary injury

c) Intratubular obstruction

d) Distal tubule dysfunction

e) Nephrogenic diabetes insipidus

PATHOGENESIS

The pathogenetic mechanisms leading to ARF can be classified into

a) DIRECT NEPHROTOXICITY DUE TO TOXINS

Administration of **Russell's Viper Venom** leads to a dose dependent decrease in inulin clearance in the isolated perfused rat kidney (Willinger *et al.,* 1995) [55]. Showed extensive destruction of the glomerular filter, lysis of vessel wall and epithelial cell injury in all segments of the tube following administration of Russell's viper venom to experimental animal.

Cyprinol, a C-27 cholesterol from raw gall bladder or bile of fresh water and grass carps is directly nephrotoxic. It is used by the traditional healers as antipyretic, anti tussive, anti hypertensive, and to improve general health in rural areas. (Lim et al., 1993)[28]. In an experimental study, oral

administration of carp bile juice power produced renal structural and functional abnormalities (Yeh *et al.,* 2002) [56].

Atractyloside, an alkaloid in the tuber of the plant callilepis laureola, produces nephrotoxicity by inhibiting oxidative phosphorylation in experimental animals (Bye *et al.,* 1990) [5].

Djenkolic acid a sulfur rich cysteine thioacetal of formaldehyde forms needle like crystals in the acid urine, causing obstruction of renal tubules. In experimental animals continuous intra venous infusion of djenkolic acid has been shown to decrease GFR in dose dependent fashion (Eiam – Ong et al., 1989) [20].

Amatoxin cyclopeptide from toxic mushrooms of the genera Amanita is directly nephrotoxic (McClain *et al.,* 1989)[31].

Semicarpus anacordium produces ARF by a phenolic substance in the sap (Mathai and Date, 1979) [30].

Chemical poisons causes direct nephrotoxic by the generation of free radicals there by causing lipid peroxidation and membrane damage.

b) INDIRECT NEPHROTOXICITY

Hypotension

Bleeding either externally or internally due to venom induced coagulation disorder or as a result of hepatotoxicity due to chemical poisons are the commonest cause of hypotension. Snake bite can also cause hypotension by releasing bradykinin, a vasodilator. Toxic myocarditis is yet another reason that leads to hypotension.

Hemolysis

Peiris *et al.*[57]observed severe and alarming hemolysis following Russell's viper bite. It results from the action of phospholipase A_2 which is present in most snake venoms and a basic p rotein called "direct lytic factor". Phospholipase A_2 causes hemolysis by direct lysis of red cell membrane phospholipids or indirectly via the production of strongly hemolytic lysolecithin from plasma lecithin.

Bee or hornet stings can cause hemolysis by direct action of a basic protein fraction and mellitenin.

Copper sulphate induced hemolysis is mainly due to oxidative mechanism.

The exact mechanism of renal failure following hemolysis is not well understood. In the mid 1940's the finding of pigment carts in the lumina of tubules led Bywaters and Stead to suggest tubular obstruction was a major factor in hemoglobinuric renal failure.

Rhabdomyolysis

Bites by sea snakes can cause severe muscle necrosis and myoglobinuria. Rhabdomyolysis in bee or hornet stings has been attributed to polypeptides, histamin, serotonin and acetylcholine present in their venoms. Myoglobinuria induced renal failure in similar to hemoglobinuria and often precipitated by dehydration and volume depletion.

Disseminated Intra Vascular Coagulation (DIC)

Disseminated intra vascular coagulation (DIC) is a consistent feature in patients bitten by several species of snake. Russell's viper venom selectively activates factor X. Sawscaled viper besides activating factor X, also accelerates conversion of prothrombin to an abnormal thrombin. This abnormal thrombin promotes coagulation, but it simultaneously prevents stabilization of fibrin both by inhibiting factor XIII activity and stimulating the plasminogen system. This phenomenon results in a clinical picture similar to that of DIC with fibrinolysis and marked consumption of clothing factor V.

The presence of fibrin thrombi in the renal microvasculature and in the glomerular capillaries, and the findings of microangiopathic hemolytic anemia and thrombocytopenia in patients with cortical necrosis strongly suggest that DIC plays a major pathogenetic role in the renal lesions (Chugh *et al.,* 1989)[15].

PATHOLOGY

In case of snake bites, kidneys are normal or slightly enlarged and then surface may show petechial hemorrhages. Light microscopy shows acute tubular necrosis in 70-80 percent or patients (Chugh 1989)[15]. The tubules are lined by flattened epithelium and the lumina contain desquamated cells and hyaline or pigment casts. Varying degrees of interstitial edema, inflammatory cell infiltration with eosinophilic, mast cells and hyperplastic fibroblasts, and scattered areas of hemorrhage may be seen. Electron microscopy reveals dense intracytoplasmic bodies representing degenerated organelles in the proximal tubules, and electron dense mesangial deposits. Acute interstitial nephritis, necrotizing vasculities involving interlobular arteries and crescentic glomerulonephritis may be seen occasionally (Sit Prija *et al.,* 1982)[49]. Acute Cortical necrosis carries the worst prognosis and in seen in about 20-25 percent of ARF cases following Russell's viper and Sawscaled viper (Chugh *et al.,* 1984)[13].

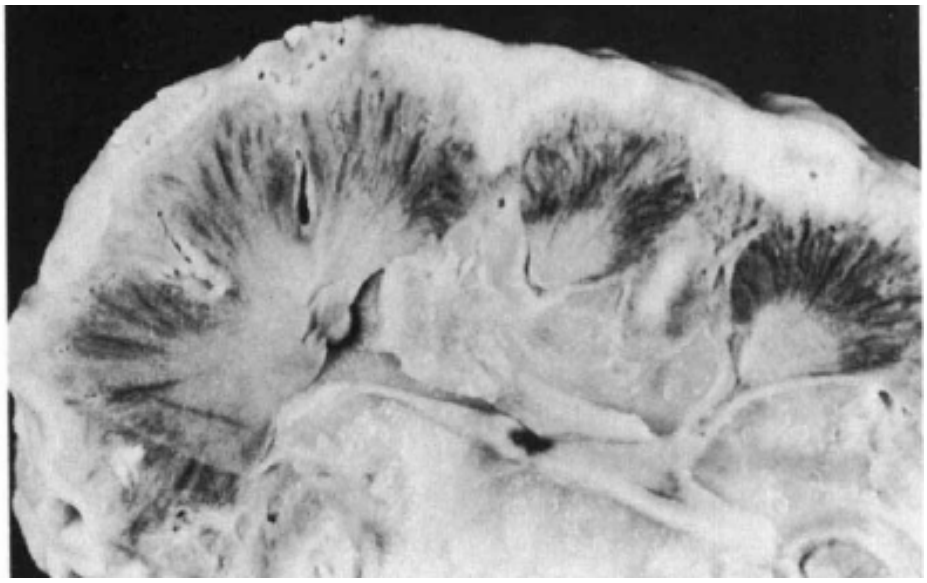


Fig. 1 : Gross appearance of a kidney from a patient who died from snake-bite-induced acute renal failure. Cortex is pale, and medulla looks dark.

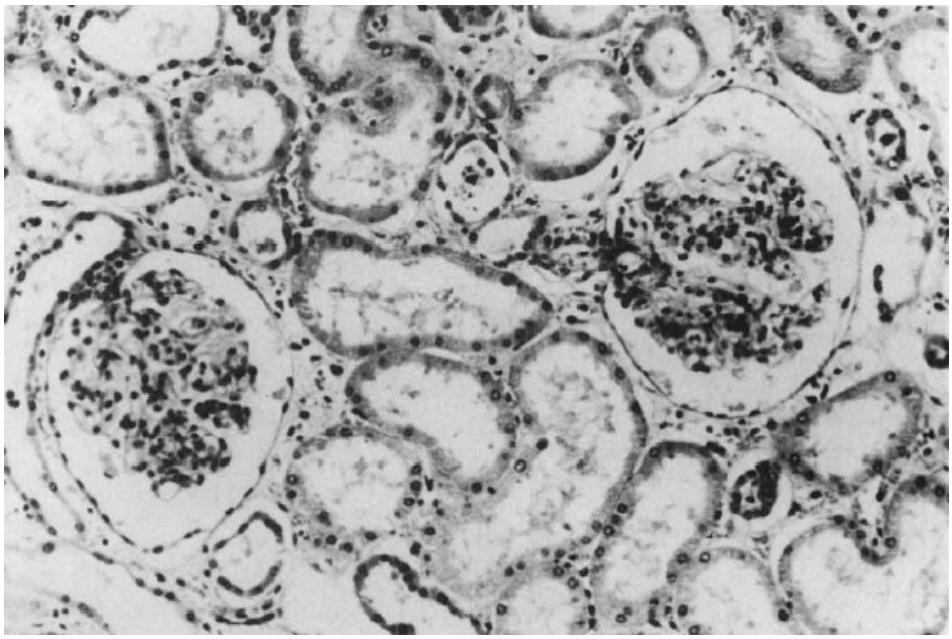


Fig. 2 : Photomicrograph showing acute tubular necrosis.

The classic pathologic feature of nephrotoxic ARF due to chemical poisoning are patchy and total necrosis of tubular epithelium with detachment from its basement membrane and occlusion of tubule lumen with casts composed of intact or degenerating epithelial cells, cellular debris, Tamm – Horsfall protein and pigment. Pigmented hemoglobin casts may be noted in patients with intra vascular hemolysis. Leukocyte accumulation is frequently observed. Rarely tubules demonstrate morphologic changes of sublethal injury, however the morphology of glomeruli and renal vascular is characteristically normal. Necrosis is most severe in the straight portion (Pars recta) of proximal tubules but may also affect medullary thick ascending limb loop of Henle (Chugh et al., 1991)[14].

CLINICAL FEATURE

Patient present with typical history of bite or poisoning. The clinical features depends on the type of poisoning. In case of envenomation by snakes, patients present with bleeding diathesis such as bleeding gums, epistaxis, malena, hemetemesis, hematuria, etc. In chemical poisoning common symptoms are related to gastrointestinal system such as vomiting, abdominal pain, loose stools, etc. They may also present with symptoms of hepatocellular failure. Patient developing acute renal failure present with decreased urine output (oliguria) that usually develops with in 48 hours of renal injury. Symptoms related to predisposing factors such as anemia, jaundice, muscle tenderness, hemoglobinuria, myoglobinuria, dehydration etc. may also be the presenting feature.

Patient may also develop symptoms of complications of ARF such as uremic encephalopathy, volume overload, acidotic breathing, cardiac rhythm disturbance and electrolyte disorders.

INVESTIGATIONS

Urine analysis

In the urine analysis pigmented muddy brown granular casts and casts containing tubular epithelial cells are characteristic of nephrotoxic ATN. They are usually found in association with microscopic hematuria and mild tubular proteinuria (< 1 g/day). The latter reflects impaired reabsorption and processing of filtered proteins by injured proximal tubules. Casts are however absent in 20-30% of the cases. Hemoglobinuria or myoglobinuria should be suspected, if urine is strongly positive for heme by dip stick, but contains few red cells and if the supernatant of centrifuged urine is positive for free heme.

RENAL FAILURE INDICES

Analysis of urine and blood biochemistry is particularly useful for distinguishing pre renal ARF from intrinsic (acute tubular necrosis) renal ARF.

TABLE - 1

URINE DIAGNOSTIC INDICES

Diagnostic Index	Typical Findings in ARF	
	Prerenal	**Intrinsic Renal**
Fractional excretion of sodium(%) $\frac{U_{Na} \times P_{Cr}}{P_{Na} \times U_{Cr}} \times 100$	< 1	> 1
Urine sodium concentration (mmol/L)	<10	> 20
Urine Creatinine to Plasma Creatinine ratio	> 40	< 20
Urine urea nitrogen to plasma urea nitrogen ratio	> 8	< 3
Urine specfici gravity	> 1.020	~ 1.010
Urine osmolality (mosmol/kg H_2O)	> 500	~ 300
Plasma BUN / Creatinine ratio	> 20	< 10-15
Renal failure index $\frac{U_{Na}}{U_{Cr} / P_{Cr}}$	<1	> 1

LABORATORY FINDINGS

Serial measurements of serum creatinine can provide useful information about the cause of ARF. Creatinine rises rapidly within 24 to 48 hours in patients with nephrotoxic ARF. In contrast creatinine peaks by 7 to 10 days in ischemic ARF. The initial rise is characteristically delayed until 2nd week of therapy with many tubule epithelial cell toxins (eg. Amino glycosides) and probably reflects the need for accumulation of these agents within the cells before GFR declines.

Hyperkalemia, hyper phosphatemia, hypocalemia, elevation in serum uric acid and creatine kinase suggest a diagnosis of Rhabdomyolysis.

A wide serum anion or Osmolal gap indicate the presence of an unusual anion or osmole in the circulation and are clues to diagnose ethylene glycol or methanol ingestion.

Severe anemia in the absence of hemorrhage raises the possibility of hemolysis.

Bleeding tendencies associated with elevated bleeding time, clotting time, prothrombin time and activated partial thromboplastin time suggest disseminated intravascular coagulation (DIC).

Gastric aspirate analysis likely to reveal the type of chemical poison mostly.

RADIOLOGIC FINDINGS

Imaging of urinary tract and measurement of kidney size by ultrasonography is useful to exclude post renal ARF and associated chronic kidney disease (CKD).

RENAL BIOPSY

Biopsy is usually reserved for patients in whom the cause of intrinsic ARF is unclear. Biopsy is not carried out routinely in ARF developing in primary causes.

COMPLICATION

Increased volume overload

Expansion of extracellular fluid (ECF) volume is an inevitable consequence of decrease salt and water excretion in oliguric or anuric patients. It is characterized by weight gain, bibasilar lung rales, increased JVP, dependent edema and life threatening pulmonary edema.

Hyper kalemia

Serum potassium rises by 0.5 mnol/L/day is oliguric patients. Coexistent metabolic acidosis exacerbate hyperkalemia by promoting potassium efflux from cells. May be severe in patients with rhabdomyolysis and hemolysis Higher potassium levels trigger cardiac arrhythmias and ECG changes.

Metabolic acidosis

Metabolism of dietary protein yields 50 to 100 mmol/d of fixed non volatile acids that are normally excreted by kidneys. ARF is complicated by high anion gap metabolic acidosis.

Hyperphosphatemia

Hyperphosphatemia may develop in highly catabolic patients or following rhabadomyolysis or hemolysis.

Hematological abnormalities

Anemia develops rapidly in ARF and is usually mild and multifactorial. Contributing factors include impaired erythropoiesis, hemolysis, bleeding, hemodilution and decreased red cell survival time.

Leukocytosis is common and are usually due to sepsis, a stress response or other concurrent illness.

Bleeding diathesis including mild thrombocytopenia, platlet dysfunction and / or clotting factor abnormalities (eg. factor VIII dysfunction) may also occur.

Infection

Infection is a common and serious complication of ARF, occurring in 50-90% of cases and accounting for upto 75% of deaths. It is unclear whether ARF patients have a clinically

significant defect in host immune responses or whether high incidence of infection reflects repeated breaches of mucocutaneous barriers. Cardio pulmonary complications of ARF include arrhythmias, myocardial infarction, pericarditis and pericardial effusion, pulmonary edema and embolism.

MANAGEMENT

Prevention

Early administration of adequate specific antivenom for bites & stings, and forced alkaline diuresis may prevent or attenuate ARF in patients suffering from rhabdomyolysis or hemolysis in copper sulphate poisoning. Ethanol inhibits ethylene glycol metabolism to oxalic acid and is an important adjunct to hemodialysis.

Supportive measures

Hypervolemia is usually managed by restriction of salt and water intake and diuretics. Metabolic acidosis in usually treated if serum bicarbonate falls below 15 mmol/L or arterial pH falls below 7.2.

Nutritional management during maintenance phase of ARF is to provide sufficient calories to avoid catabolism and starvation ketoacidosis, while minimizing the production of nitrogenous waste. Restricting dietary protein to 0.6 g / kg / day of high biologic value and to provide most calories as carbohydrate.

Anemia

Anemia necessitate blood transfusion, if severe or if recovery is delayed. In contrast to CKD, recombinant human erythropoietin is rarely used in ARF, because marrow resistance to erythropoietin is common. Uremic bleeding usually responds to correction of anemia, administration of desmopressin or estrogen or dialysis.

Infection

Meticulous care of intravenous cannulae, bladder catheters and other invasive devices is mandatory to avoid infections. Unfortunately, prophylactic antibiotic have not been shown to reduce the incidence of infection in these patients.

WHAT TO AVOID IN ACUTE TUBULAR NECROSIS

a) High dose diuretics :

No data support the use of high dose diuretic therapy in established ATN. Frusemide and other loop diuretics are frequently used in oliguric ARF in an effort to convert it to non oliguric ARF. Although the conversion of oliguric to non oliguric renal failure many simplify fluid management, clinical trials have failed to demonstrate that the use of diuretics in associated with improved outcome in patients with ARF (Eddie Needham *et al.,* 2005) [18].

b) Renal – dose dopamine

Dopamine is a selective renal vasodilator. It elicits profound natriuresis and increases urine output. The renal selective dose in 1-3 mcg per Kg per minute. No evidence suggests that renal dose dopamine is beneficial in ARF. In fact, several studies have identified deleterious effects, such as bowel ischemia and arrhythmias. Unless dopamine is required for circulatory support, it should not be used for ARF (Denton *et al.,* 1996) [19].

c. Nephrotoxic drugs

Potentially nephrotoxic drugs and agents should be avoided in ARF, because they may perpetuate the renal injury. These agents and drugs include NSAIDS, ACE inhibitors, cyclosporine, tacrolimus, aminoglycosides, radiocontrast agents and amphotericin B.

d. Volume Overload

The amount of intravenous fluids necessary for critically ill patients is unknown, and intravenous fluids must be given judiciously in the setting of ATN, especially if the patient is oliguric. In general, the fluids should not contain potassium.

Renal replacement therapy (RRT) - Dialysis

Renal replacement therapy is required when kidney function deteriorates to the point where the accumulation of waste products begin to interfere with life function. Dialysis replaces renal function until regeneration and repair restore renal function.

Indications

- Symptoms or signs of uremic syndrome

  (eg. Encephalopathy, Pericarditis)

- Refractory hypervolemia
- Hyperkalemia (serum potassium greater than 6.5 mEq. per dL)
- Metabolic acidosis
- Blood urea nitrogen greater than 100 mg per dL.
- Serum creatinine higher than 6 mg per dL.

Type of dialysis

The dialysis modality is chosen according to the needs of individual patients, the expertise of the nephrologists and the facilities of the institution. The main modalities of dialysis are intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT).

Intermittent hemodialysis is typically used in otherwise stable patients who can tolerate rapid fluid removal. In this form of dialysis, patient is connected to a dialysis machine for 4 hours at a time, daily or every second day. The

technique requires a double-human catheter, tubing, hemodialysis machine, a dialysis membrane and a dialysis nurse. Vascular access is achieved by insertion of temporary double lumen catheter into the internal jugular vein. The sub clavian and femoral vein are alternative access sites. Daily treatment for 4 hours with a blood urea clearance of 200 ml per minute, can achieve a weekly urea clearance of 350 litre. The dose and frequency of dialysis for ARF may need to be higher than in the chronic setting, because ARF patients are typically hypercatabolic and most temporary catheters have a high recirculation rate. Recent evidence suggest that more intensive hemodialysis (daily rather than alternate day) is clinically superior and confers improved survival in ARF (Schiffl

et al., 2002) [40].

Continuous renal replacement therapies (CRRT)

They are particularly valuable in patients in whom intermittent dialysis fails to control hypervolemia or uremia and for those who do not tolerate intermittent hemodialysis and in whom peritoneal dialysis is not possible.

Types

- Continuous arterio venous hemodiafiltration (CAVHD)
- Continuons veno venous hemodiafiltration (CVVHD)
- Continuous arterio venous hemofiltration (CAVH)
- Continuons veno venous hemofiltration (CVVH)

Advantages of CRRT is as the removal of solutes and fluids is slow and continuous, hemodynamic instability and hypotensive episodes are reduced. Minimization of hypotension, theoretically avoids perpetuation of Renal injury.

Disadvantages of CRRT are need for prolonged immobilization in bed, systemic anticoagulation, arterial cannulation and prolonged exposure of blood to synthetic, albeit relatively biocompatible dialysis membrane.

Peritoneal dialysis

Peritoneal dialysis appears equally effective. It may be an option in location where IHD or CRRT is not available. It is indicated in patients with minimally increased catabolic state without an immediate or life threatening indication. It is ideal for hemodynamically unstable patients. For short term dialysis, a rigid dialysis catheter is inserted into the peritoneum, through the anterior abdominal wall, 5 to 10 cm below the umbilicus. Exchanges of 1.5 to 2.0 litre of standard peritoneal dialysis solutions are infused into the peritoneum.

Outcome & prognosis

The mortality rate among patients with toxin related ARF is approximately 30%. If should be stressed, however that patients usually die from sequelae of primary illness that induced ARF and not from ARF itself. Mortality rates are higher in older individuals and in those with multiple organ failure. 50% have subclinical impairment of renal function on residual scanning or biopsy. 5% of patient never recover function and require long term renal replacement with dialysis

or transplantation. Additional 5% suffer progressive decline in GFR following an initial recovery phase, probably due to hemodynamic stress and sclerosis of remnant glomeruli (Cherlow et al., 1996 and Levy Em et al., 1996) [7].

Materials and Methods

MATERIALS AND METHODS

Study Population

In this prospective analytical study 1250 cases admitted in Poison Control, Training and Research Centre of Government General Hospital, Madras Medical College over a period of consecutive 12 months i.e. from August 2006 – July 2007. They were evaluated and monitored for development of acute renal failure.

Data Collection

Their socio demographic, clinical, laboratory parameters and outcome were collected. Demographic data included age of the patient, sex, date and time of hospitalization and reason for delay in hospitalization if present.

Clinical data were symptoms related to the primary etiology, renal failure and its predisposing factors or involvement of other organs were recorded in detail. Past history of any other diseases contributing to chronic kidney diseases were elicited.

Laboratory parameters included complete blood count, peripheral smear, urine analysis, blood urea, serum creatinine, serum electrolytes and whole blood clotting time.

All the 32 patients were followed till discharge from the hospital.

Methodology for Estimation

Blood urea	-	Ultra violet method
Serum creatinine	-	JAFF's picric acid method
Urine for albumin	-	Sulphosalicylic acid method

Sample size

32 patients.

Inclusion Criteria

1. Patient with normal serum creatinine at admission and subsequent values elevated (as defined by RIFLE criteria).

2. Patient with elevated serum creatinine at admission with no history suggestive of any predisposing factors

that would have caused chronic kidney disease and normal size kidneys in the ultrasound.

EXCLUSION CRITERIA

1. Patient with history of diabetes/ hypertension
2. Known chronic kidney disease.
3. Chronic NSAID's therapy.
4. Patient on drugs that increases serum creatinine by inhibiting creatinine secretion.

    a) Trimethoprim
    b) Cimetidine
    c) Probenecid
    d) Triamterene
    e) Amiloride
    f) Spironolactose

Period of study

One year (Aug 2006 – July 2007).

Type of study

Simple prospective analytical study

Statistical Analysis

Chi-square test.

Ethical clearance

Enclosed.

Informed consent

Obtained

Conflict of interest

Nil

Financial Support

Nil

Limitation

Renal biopsy not done.

Results

RESULTS

There were 1250 cases admitted in our toxicology training and research centre during one year. Of which, 32 cases developed ARF and they were included in the study.

TABLE – 2 : PREVALENCE OF ARF IN POISONING

Etiology	Total No. of Cases	Cases of ARF (%)	Death due to ARF
Organo phosphorus poisoning	400	Nil	-
Russell's viper bite	120	22 (18)	5
Other snake bite	193	Nil	-
Scorpion sting	70	1 (1)	-
Wasp sting	7	1 (14)	-
Copper sulphate	20	2 (10)	2
Rat Killer	140	2 (1.4)	2
Other chemical Poisons (Dichromate Indigenous medicine Vasmol 33, etc.)	150	4 (2)	3
Tablet poisoning	150	Nil	-
Total Cases	**1250**	**32 (2.5)**	**12**

ARF = Acute renal failure

Table –2 shows the prevalence of ARF in poisoning cases. Out of 313 cases of snake bite 22 cases (7%) developed renal failure and all these 22 were bitten by Russell's viper, the only species that caused ARF in snake bite cases. Out of 120 cases 22 cases developed ARF (18%) and were due to Russell's viper bite alone. Only one cases of scorpion sting and wasp sting developed renal failure. In the chemical poisoning, copper sulphate and rat killer were the commonest cases that developed ARF in our centre. Organo phosphorous poisoning though the most common in the number of admission, none of the cases developed ARF. Other chemical poisoning that developed ARF were dichromate, indigenous medicines and vasmol 33 (paraphenelyne diamine) one each case.

The clinical and lab parameters among ARF due to bite & stings and chemical poisoning are provided in Table - 3. Among 32 cases 24 cases were due to bites and stings. The average age was 40.7 years.

TABLE 3 : CLINICAL & LAB PARAMETERS AMONG POISONING

Parameters	Bites & Stings	Chemical Poisoning
Average Age	40.7	33
Time of onset of oligoanuria	18-96 hours	24-96 hours
Oliguria	20/24	6/8
Albuminuria	20/24	0/8
Intra vascular hemolysis	10/24	2/8
Hepatic failure	0/24	7/8
Urea		
Serum creatinine	6.1 ± 4.7	
Average period of stay	14-21 days	3-4 days
Dialysis	18/24	8/8
Mortality	5/24	7/8

The time of onset of oligoanuria ranged from 18-96 hours. Most common symptom due to renal dysfunction was

oliguria and was present in 83%of cases. Hemolysis is the most common predisposing factor that increased the severity of the renal failure and was observed in 41% of cases.

On investigation, all the 22 cases of snake bite revealed to have whole blood clotting time of more than 20 minutes. In the urine analysis albuminuria was found in 83% of cases. The mean blood urea and serum creatinine was found to be 130 ± 51 and 6.1 ± 4.7 respectively. 75% of the cases were taken for renal replacement therapy and the remaining 25% were managed conservatively. The average period of stay in the hospital varied from 14 to 21 days. The mortality among ARF due to bites and stings was 21%.

Of the 310 cases of chemical poisoning, ARF was noticed in eight cases and the chemical composition was confirmed to be as copper sulphate into one due to paraphenelyne diamine and an another due to potassium dichromate. The average age of presentation was 33. The time of onset of symptoms were equal to bites and stings. Similar to bites and stings most

common symptom of renal dysfunction was oliguria and was observed in 6 out of these 8 cases of chemical poisoning.

In contrast to bites and stings, the most common predisposing factor was found to be hepatic failure and was present in 7 out of 8 cases. On investigation, none of the cases of ARF due to chemical poisoning had albuminuria. The average blood urea and serum creatinine among them were 150 ± 33 and 6.8 ± 0.8 respectively. All these 8 cases needed renal replacement therapy and 7 out of 8 cases expired due to multiple complications.

The predictors of outcome were classified as etiology, predisposing factors i.e. hemolysis in bites and stings and hepatic failure in chemical poisoning, serum creatinine, age of the patient and time of onset of oligoanuria.

In the present study, the cases of ARF due to bites and stings had better prognosis than chemical poisoning and the difference was highly significant at 1% level ($P < 0.001$).

Similarly presence of predisposing factors led to a poor outcome and the difference was highly significant at 1% level (P=0.008) as shown in the Table 4 given below.

On the other hand, age of the patient, time of onset of oligoanuria and serum creatinine level has no influence on the outcome.

TABLE – 4

PREDICTORS OF OUTCOME IN THOSE WITH ARF

(N=32)

Factors		Improved	Death	P values
Etiology	Bites & Stings (N=24)	19	5	0.001
	Chemical poisoning (N=8)	1	7	
Predisposing factors	Present (N=19)	8	11	0.008
	Absent (N=13)	12	1	
Serum creatinine in mg %	> 6.4 (N=12)	6	6	0.258
	< 6.4 (N=20)	14	6	
Age in years	> 40 (N=18)	11	7	0.854
	< 40 (N=14)	9	5	
Time of onset of oligoanuria in hours	< 24 (N=11)	6	5	0.501
	> 24 (N=21)	14	7	

GRAPHS

FIG. 3

DISTRIBUTION OF ARF AMONG POISON CASES

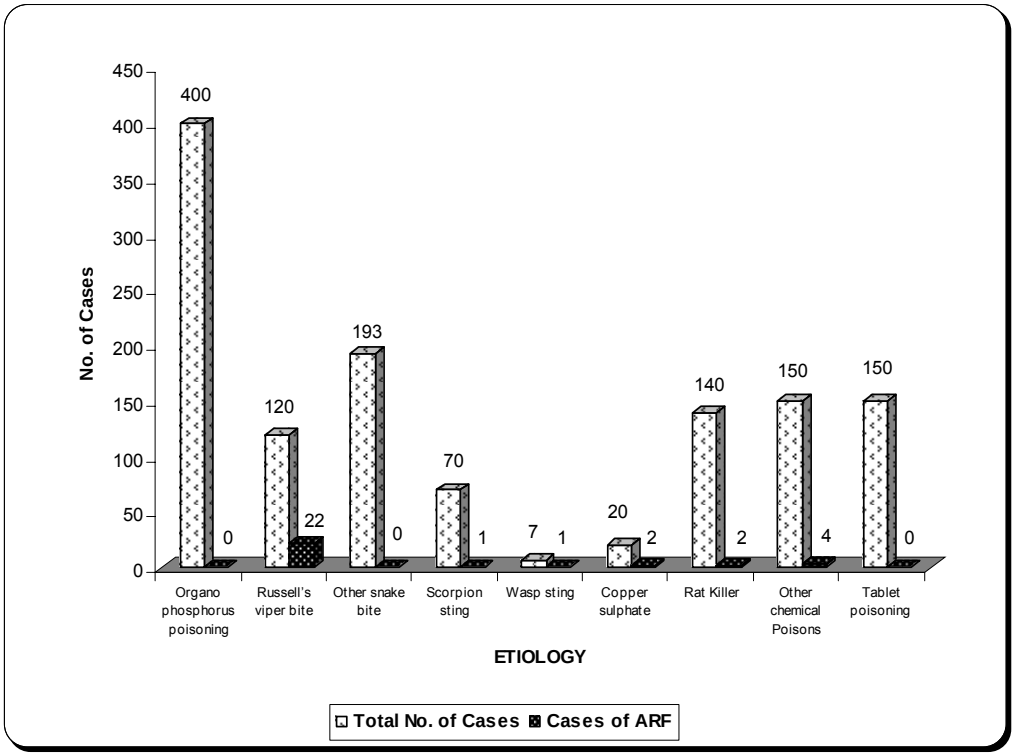


FIG. 4

OUTCOME IN RELATION TO THE TYPE OF POISON

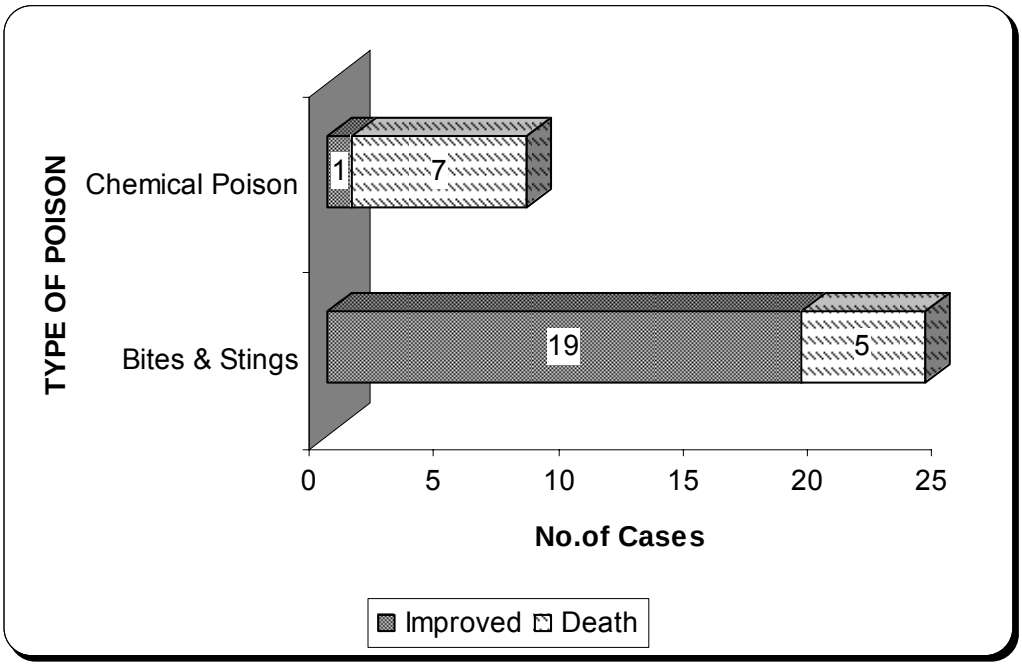
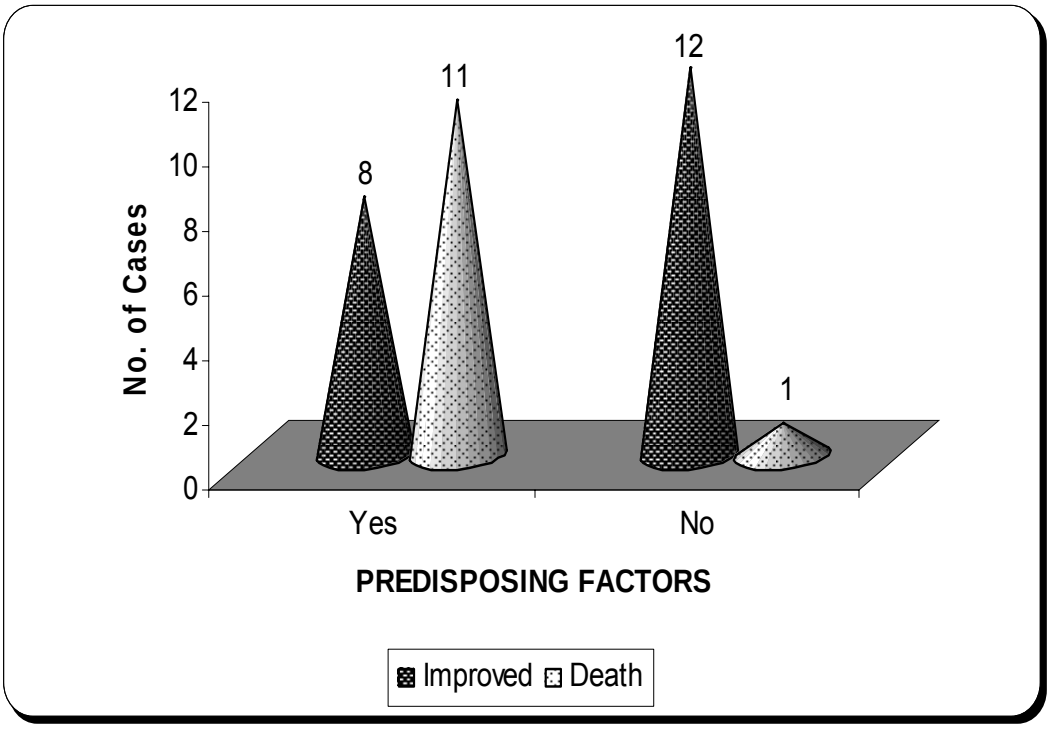


FIG. 5

OUTCOME IN RELATION TO PREDISPOSING FACTORS



Discussion

DISCUSSION

Widespread human exposure to a variety of drugs, chemicals, and biologic products and recent awareness of their toxic manifestations has led to the recognition of toxic nephropathy as an important segment of renal disease in the tropical countries. Tropical nephrotoxins are distinctly different from those seen in the rest of the world and are derived from local fauna and flora or plant and chemical sources. The spectrum of exposure varies from country to country and even from community to community, depending on variations in the distribution of local plants and animal species and prevalent social practices. Acute renal failure (ARF), either alone or in association with liver failure, neurologic abnormalities, metabolic acidosis, disseminated intravascular coagulation, or pulmonary infections is the most common form of presentation.

Traditional medicines prescribed by witch doctors (traditional healers) constitute a special class of nephrotoxins among several communities in Africa and Asia. The prevalence of nephropathy caused by traditional medicines is directly related to a combination of ignorance, poverty, lack of medical

facilities, lax legislation, and widespread belief in indigenous systems of medicine in rural areas. These medicines are a mix of herbs and unknown chemicals administered orally or as enemas. Clustering of cases after exposure to a particular agent suggests the possibility of a toxic insult.

Common animal nephrotoxins are venoms of viper snakes, sea snakes, stinging insects, and raw gallbladder and bile of carp and sheep. Botanical nephrotoxins are encountered both in common edible plants (djenkol beans, mushrooms) and medicinal herbs (impila, cat's claw). Mistaken identification of medicinal herbs by untrained workers and even deliberate trials of toxic substitutes derived from plants frequently lead to renal disease, the most commonly reported being the Chinese herbal nephropathy. Nephrotoxicity caused by chemicals can be secondary to accidental occupational exposure in industrial work places (eg, chromic acid), or after suicidal or homicidal use (eg, copper sulphate, ethylene dibromide, ethylene glycol). Late presentation and multiorgan dysfunction are associated with a high mortality. A high index of suspicion, careful history taking, and an awareness of local practices are essential for proper diagnosis and management of toxic nephropathies in the tropics.

BITES & STINGS

Demography

Snake bite is known to man since antiquity. It constitutes a significant cause of mortality in tropical countries. The annual mortality rate in around 30,000, most of them from South-East Asia and West Africa. Approximately 10,000 deaths occur in India (Chatterjee et al., 1965 and Reid et al., 1983)[6, 39].

Acute renal failure is mainly observed following bites by Viperidae group, sea snakes and colubridae group, but the substantial proportion of these cases result from viper bites. [Chugh et al., 1984) [13].

In our study 18 percent (22 out of 120 cases) admitted to poison control unit developed renal failure following Russell's viper bite. This is comparable with the incidence of ARF in Chugh et al. (1984) study[13]and Shastry et al. (1977)[44] which varies from 13 to 22% following Sawscaled viper or Russell's viper. Also the Mittal et al. (1994)[32] study had a similar incidence of 16.2% of ARF following Russell's viper bite.

22 cases due to snake bite induced renal failure were included in this study. Their average age was 40.7 years, the youngest patient was 14 years and the oldest 63 years old. The snake was identified as Russell's viper in all 22 cases. Identification of snake was based on the actual examination of snake brought by the patient or witness, supported by the clinical features of envenomation. Exact identification of snake was not possible in 12 cases. However, those patients had renal manifestation and bleeding diathesis followed the bite. Along with clinical manifestation and the description made by the patients were all suggestive of snake bite due to Viperidae group.

Clinical manifestation and investigation analysis

In the Chugh et al. (1989)[15] study oligoanuria generally develops within a few hours to as late as 96 hours and 94% of the patients had oligoanuria. In the present study also oligoanuria developed within few hours i.e. 18 hours to 96 hours after bite, and 80 percent (18 out of 22 cases) developed the symptoms.

Hematological abnormalities

Hemolysis is an important manifestation observed in Russell's viper bite, which induced ARF. It has been reported to be present in more than 50% of patients with ARF. It results from the action of phospholipase A2 and direct lytic factor present in the venom. Chug *et al.* (1989)[15] noticed hemolysis in 54% of patients with snake bite induced renal failure. In the present study hemolysis was noticed in 10 of the 22 (45%) cases which was evidenced by sudden decrease in Hemoglobin with no evidence of internal or external hemorrhage associated with jaundice, raised serum lactate dehydrogenase and peripheral smear.

Coagulation abnormalities are common in Sawscaled viper and Russell's viper bite due to the activation of Factor X and thrombin. In the present study prolonged whole blood clotting time of > 20 minutes was observed in 100 percent (all the 22 cases with ARF). Among them 27% (6 out of 22 with ARF) presented with spontaneous mucosal bleeding.

Complete coagulation profile could not be carried out due to technical constraints.

Renal Function Abnormalities

Albuminuria found only in patients who became systemically envenomed, was associated with high fractional excretion of sodium in those who developed acute oliguric renal failure. Albuminuria may appear before a gross clotting defect. Spot measurement might prove a useful early predictor of outcome (Thein-Than et al., 1991)[52].

Albuminuria is early predictor of systemic envenomation and there by indicates generalized increase in capillary permeability (WHO guidelines for the management of snake bite in Southeast Asia Region)[54]. In our study 86 percentage of patients (19 out of 22 cases) had albuminuria which was in concurrence with Thein-Than et al., (1991) study [52].

In the Mittal et al. (1994)[32] study patients, serum creatinine ranged from 1.5 to 20 mg %, but they did not find any correlation between the highest value and survival.

During the present study the serum creatinine ranged from 2.4 to 18.7 mg % with a mean of 6.1 mg %. There was no correlation between serum creatinine and survival ($P<0.01$).

Another limitation in our study was non performance of renal biopsy in any of the patients and it was due to non willing and ethical guidelines. Only one out of 22 cases developed end stage renal disease which might be due to bilateral cortical necrosis and he was included for the maintenance hemodialysis programme.

Management

The basic therapeutic approach for acute renal failure in patients bitten by snakes was the same as that for acute renal failure of any other cause. But several problems other than renal failure can pose an immediate threat to the life of an envenomed patient. These include bleeding, coagulation disturbances shock and sepsis.

Early administration of antivenom is a vital therapeutic measure. Polyvalent antivenom is the most common antidote

used in the tropical countries. Bhat observed the requirement of anti-snake venom from 60 to 270 ml of Kasauli polyvalent cobra-krait-viper venom to reverse the clotting defect (Bhat, 1974)[3]. Chugh et al. (1984)[9] in his study has proved that timely administration of antivenom has been shown to completely reverse all clinical manifestations of systemic envenomation.

In the present study only 13 percentage (3 out of 22 cases) had received adequate treatment ie., at least 60 ml of polyvalent anti venom as per Bhat et al. (1974)[3] before hospitalization in our centre.

Common reason that precludes the patients in getting appropriate treatment were poverty, lack of medical facilities, socio cultural beliefs and management by traditional healers or witch doctors.

Apart form anti snake venom, blood products were given for persistent coagulation abnormalities. In this institution hemodialysis remains the main stay of treatment of patients developing renal failure. Peritoneal dialysis is used in

hemodynamically unstable patients and in patients on mechanical ventilation.

The period of dialysis ranged from 14 to 21 days, on alternate days, though the recent evidence suggest that more intensive daily hemodialysis rather than alternate day, which was found to be superior and have improved survival in ARF (Schiffl et al., 2002)[40].

Outcome and Prognosis

Renal failure is one of the common cases of death in snake bite. The severity of acute renal failure in viper envenomed patients is determined by the venom dose and the severity of bleeding, hypotension, hemostatic abnormalities and intravascular hemolysis (Chugh et al., 1989) [15].

The mortality from snake bite induced acute renal failure in our study was 22 percent (5 out of 22 cases) that is consistent with Chugh et al. (1989) [15] study with the mortality rate of 28% and 25% mortality rate in the Ali et al. (2004)[1] study.

CHEMICAL POISONING

The incidence of chemical poisoning varies at different geographical areas depending on the local use of the substance and the availability of other suicidal poison.

In our study only 8 cases of chemical poisons developed ARF. Most common was due to copper sulphate poisoning.

Copper Sulphate Poisoning

Chuttani et al. (1965)[17] observed prevalence of 34% of copper sulphate poisoning among the total poisoning cases. In the present study the prevalence of copper sulphate poisoning was only 1.6 % among the 1250 cases. This may be due to the geographical variation and the materials preferred or available to the victim.

Chugh et al. (1989)[15] observed ARF among 1% of copper sulphate poisoning, but in the present study, ARF among 10% of cases. Though it was quite high, it was not statistically comparable with the above study as the number of copper sulphate poisoning induced ARF was only two cases.

Kavitha Saravu et al. (2007)[27] studied renal complications in copper sulphate poisoning which was developed after 48 hours. In the present study too renal dysfunction developed only at the end of second day in two of the 20 cases.

Chuttani et al. (1965)[17] observed a mortality rate of 14% in copper sulphate poisoning and the major factors influenced the mortality were hepatic and renal dysfunction in predialysis era.

In the present study 2 out of 20 cases (10%) died due to combined hepatic and renal failure within 3-4 days of poisoning despite one were provided with intensive hemodialysis and other was given peritoneal dialysis due to hemodynamic instability.

Hair dye poisoning

The compound in Vasomol 33 in our study was identified to be paraphenylene diamine. Similar case was observed by Chugh et al. (1983)[12]. They had 2 cases of hair dye poisoning,

both developed renal failure. Inspite of dialysis, one patient died due to septicemia. In the present study only one case was due to hair dye poisoning and died on the second day due to combined hepatic and renal dysfunction.

Potassium dichromate poisoning

In the present study the patient with potassium dichromate poisoning developed ARF after 24 hours associated with Gastrointestinal bleeding and circulatory collapse and expired inspite of dialysis. A similar case report was published by Sharma et al. (1978)[45].

As the cases admitted with ARF due to chemical poisoning in our centre were smaller in number, we were unable to do a comparative study based on early publications.

Conclusion

CONCLUSION

1. The prevalence of ARF among the cases of poisoning was 2.5%.
2. In the present study, among the big four (Russell's viper, Sawscaled viper, Krait and Cobra) ARF was observed only in Russell's viper bite. Eighteen percent of Russell's viper bite went in for ARF.
3. Among 20 cases of copper sulphate poisoning two developed ARF (10%) and both expired.
4. The less common causes of ARF were one each following scorpion bite, wasp bite, hair dye, dichromate and indigenous medicine and two due to rodenticide.
5. The commonest predisposing factor for ARF in bites & stings was hemolysis, and that of chemical poisoning was hepatic failure.
6. Albuminuria was noticed in snake bite before the onset of overt renal dysfunction.
7. The predisposing factors adversely affected the outcome.

8. Patients with ARF due to bites and stings improved well than chemical poisoning.

Bibliography

BIBLIOGRAPHY

1. Ali, G., M Kak, M Kumar, S.K Bali, SI Tak, G Hassan, MB Wadhwa (2004). Acute renal failure following echis carinatus (saw – scaled viper) envenomation. *Indian J Nephrol*;**14**: 177-181.
2. Anon (1996). Fatalities associated with ingestion of diethylene glycol-contaminated glycerin used to manufacture acetaminophen syrup-Haiti, November 1995 – June 1996. *Morbidity and Mortality Weekly Report,* **45**, 649-650.
3. Bhat RN (1974). Viperine bite poisoning in Jammu. *J. Indian Med. Assoc.,* **62** : 383-392.
4. Burdmann, E.A. et al.(1993). Snake bite-induced acute renal failure : an experimental model. *American Journal of Tropical Medicine and Hygiene*, **48**, 82-88.
5. Bye, B.N., T.H. Coetzer, and M.F. Dutton (1990). An enzyme immuno assay for atractyloside, the nephrotoxin of callilepis laureola. *Toxicon*, **28**, 997-1000.

6. Chatterjee S.C. (1965). Management of Snake bite cases. *J. Ind. Med. Assoc.,* **45** : 654.

7. Chertow et al. (1996). *Prognostic Stratification in Critically ill patients with ARF requiring dialysis Arch Internal Med.* **155**(14) : 1505-11.

8. Chugh KS, GH, Malik and PC. Singhal (1982). Acute renal failure following paraphenylene diamine [hair dye] poisoning: report of two cases. *J. Med*., **13(1-2)** : 131-7.

9. Chugh KS, Pal Y, Chakranarhy RN, Datta BN, Mehta R, Sabhiya R, Navel AK, Sommers SC, et al (1984). Acute renal failure following poisoning snake bite. *Am. J. Laid Dis.,* **40** : 30-38.

10. Chugh, K.S. (1989). Snake bite – induced acute renal failure in India. *Kidney international*, **35**, 891-907.

11. Chugh, K.S. et al. (1978). Spectrum of acute renal failure in North India. *Journal of Association of Physicians of India*, **26**, 147-154.

12. Chugh, K.S. et al. (1983). Spectrum of cortical necrosis in Indian patients. *American Journal of Medical Sciences*, **286**, 10-20.

13. Chugh, K.S. et al. (1984). Acute renal failure following poisonous snake bite. *American Journal of Kidney Diseases*, **4,** 30-38.

14. Chugh, K.S., S. Sakhuja, V., and Pereira, B.J.G. Acute renal failure in the tropics. In *Acute Renal Failure* (ed. K. Solez and L.C. Racusen), pp.93-103. New York : marcel Dekker, 1991.

15. Chugh, K.S., Sakhuja, V. Malhotra, H.S., and Pereira, B.J.G. (1989). Changing trends in acute renal failure in third world countries – Chandigarh study. *Quarterly Journal of Medicine,* **73**, 1117-1123.

16. Chugh, K.S., Sharma, B. K., Singhal, P.C., Das, K. C., and Datta, B.N. (1977a). Acute renal failure following copper sulphate intoxication. *Postgraduate Medical Journal*, **53**, 18-23.

17. Chuttani HK, P.S. Gupta, S. Gulati and D.N. Gupta (1965). Acute copper sulphate poisoning. *Am. J. Med.* **39** : 849-54.

18. Eddie Needham et al. (2005). High dose diuretics and acute renal failure. *Am. Fam Physician*, **72,** 1739-46.

19. Denton MD et al. (1996). Renal-dose: dopamine for the treatment of acute renal failure : Scientific rationale, experimental studies and clinical trials. *Kidney Int.,* **49** :4.

20. Eiam – Ong, S. et al. (1989). Djenkol bean nephrotoxicityin Southern Thiland. *Proceedings of the First Asia Pacific Congress on Animal, Plant and Microbial Toxins, Singapore*, pp.628-632.

21. Gold, C.H. (1980). Acute renal failure from herbal and patent remedies in Blacks. *Clinical Nephrology,* **14**, 453-454.

22. H'ng, P.K., Nayar, S.K. Lau, W. M., and Segasothy, M. (1991). Acute renal failure following jering ingestion. *Singapore Medical Journal* **32**, 148-149.

23. Haberman, E. (1977). Bee and Wasp venoms. *Science* **177**, 314-322.

24. Hanif, M., Mobarak, M. R., Ronan, A., Rahman, D., Donovan, J. J., Jr. and Bennish, M.L. (1995). Fatal renal failure caused by diethylene glycol in paracetamol elixir :

The *Bangladesh epidemic. British Medical Journal*, **311**, 88-91.

25. Jha, V., Malhotra, H.S., Sakhuja, V., and Chugh, K.S. (1992). Spectrum of hospital – acquired acute renal failure in the developing countries- Chandigarh study. *Quarterly Journal of Medicine,* **84,** 497-505.

26. Joubert, P. and Sebata, B. (1982). The role of prospective epidemiology in the establishment of a toxicology service for a developing community. *South African Medical Journal*, **27**, 63-67.

27. Kavitha Saravu, Jimmy Jose, Mahendra N Bhat, Beena Jimmy and B.A. Shastry (2007). *Indian J. Crit. Care Med. Apr.,* **11 (2)**.

28. Lim, P.S., Lin, J.L., Hu, S. A., and Huang, C.C. (19930. Acute renal failure due to ingestion of the gallbladder of grass carp: report of 3 cases with review of literature. *Renal Failure* **15**, 639-644.

29. Lin, Y.F. and Lin, S.H.(1999). Simultaneous acute renal and hepatic failure after ingesting raw carp gall bladder. *Nephrology, Dialysis, Transplantation* **14,** 2011-2012.

30. Mathai, T.P. and Date, A.(1979). Renal cortical necorsis following exposure to sap to the marking nut tree *(Semecarpus anacardium_. American journal of Tropical Medicine and Hygiene*, **28**, 773-774.

31. McClain, J. L., Hause, D.W., and Clark, M.A. (1989). *Amanita phalloides* mushroom poisoning : a cluster of four fatalities. *Journal of Forensic Sciences*, **34**, 83-87.

32. Mittal, B.V., (1994). Acute renal failure following poisonous snake bite. *Journal of Post Graduate Medicine,* **40(3)** : 123-126.

33. Munoz-Arizpe, R. et al. (1992). Africanized bee stings and pathogenesis of acute renal failure. *Nephron* **61**, 478.

34. Muthusethupathi, M.A. and Shivakumar, S. (1987). Acute renal failure in South India. *Journal of the Association of Physicians of India,* **35**, 504-508.

35. Otieno, I., S., McLigeyo, S.O., and Luta, M.(1991). Acute renal failure following the use of herbal remedies. *East African Medical Journal* **68**, 993-998.

36. Park, S.K. et al. (1990). Toxic acute renal failure and hepatitis after ingestion of raw carp bile. *Nephron,* **56**, 188-193.

37. Pereira, B.J.G. Pereira, S., Gupta, A., Sakhuja, V. and Chugh, K.S. (1989). Acute renal failure in infants in the tropics. *Nephrology, Dialysis, Transplantation* **4**, 535-538.

38. Prakash M.S., Sud, K., Kohli, H. S., Jha, V., Gupta, K.L. and Sakhuja, V. (1999). Ethylene dibromide poisoning with acute renal failure : first reported case with non-fatal outcome. *Renal Failure* **21**, 219-222.

39. Reid HA, Theatson RDG (1983). Management of Snake bite. *Bull WHO,* **61** : 888.

40. Schiffl H et al. (2002). Daily hemodialysis and the outcome of acute renal failure. *N. Engl. J. Med.,* **346** : 305.

41. Sert, M. Tetiker, T. and Paydas, S. (1993). Rhabdomyolysis and acute renal failure due to honeybee stings as an uncommon cause. *Nephron,* **65**, 647.

42. Sesagothy, M., Swaminathan, M., King, N.C.T. and Bennett, W.M. (1995). Dienkol bean poisoning (Djenkolism) : an unusual cause of acute renal failure. *American Journal of Kidney Diseases.* **25**, 63-66.

43. Shah, P.P. Trivedi, H. L., Sharma, R.K. Shah, P.R., and Joshi, M.N. (1985). *Acute renal failure, experience of 816 patients in the tropics. Abstracts of the XVth Annual Conference of the Indian Society of Nephrology*, Bangalore, p.17.

44. Shastry JCM, Datea, Carman RH, Jony KV (1977). Renal failure following snake bite. *Am. J. Trop. Med. Hyg.* **26**; 1032-38.

45. Sharma, B.K., P.C. Singhal and K.S. Chugh (1978). Intravascular haemolysis and acute renal failure following potassium dichromate poisoning. *Post graduate Medical Journal,* **54**; 414-45.

46. Singh, J. et al. (2001). Diethylene glycol poisoning in Gurgaon, India, 1998. *Bulletin of World Health Organization*, **79**, 88-95.

47. Singh, S., Chuadhary, D., Garg, M., and Sharma, B.K. (1993). Fatal ethylene dibromide ingestion. *Journal of Association of Physicians of India*, **41**, 608.

48. Sitprija, V. and Benyajati, C.(1975). Tropical diseases and acute renal failure. *Annals of the Academy of Medicine of Singapore* **4** (Suppl.), 112-114.

49. Sitprija, V., Suvanpha, R., Pochngool, C. Chusil, S. and Tungsanka, K. (1982). Acute interstitial nephritis in snake bite. *American Journal of Tropical Medicine and Hygiene,* **31**, 408-410.

50. Sontz, E. and Schweiger, J. (1995). The 'Green Water' syndrome : copper-induced hemolysis and subsequent acute renal failure as consequence of a religious ritual. *American Journal of Medicine* **98**, 311-315.

51. Tariang, D.D. et al. (1999). Randomized controlled trial on the effective dose of anti-snake venom in cases of snake bite with systemic envenomantion. *Journal of Association of Physicians of India,* **47**, 369-371.

52. Thein – Than et al. (1991). Development of renal function abnormalities following Russell's viper bite in Myanmar.

Transaction of Royal society of tropical medicine and hygiene. Vol. **85** (3), May, 404-409.

53. Warell D.A. (1989). Snake venoms in science and clinical medicine. 1. Russell's viper : biology, venom and treatment of bites. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **83**, 732-740.

54. Warrell, D.A., (1999). WHO/SEARO guidelines for the clinical management of snake bites in the sotaheast Asian region. *Southeast Asian Journal of Tropical Medicine and Public Health,* **30** (Suppl. 1), 1-85.

55. Willinger, G.G., Thamaree, S., Schramek, H., Gstraunthaler, G. and Pfaller, W. (1995). *In vitro nephrotoxicity of Russell's viper venom*. *Kidney International* **47**, 518-528.

56. Yeh, Y.H., Wang, D.Y., Deng, J.F., Chen S.K. and Hwang, D.F. (2002). Short-term toxicity of grass carp bile powder, 5slpha-cyprinol and 5slpha-cryprinol sulfate in rates. *Comparative Biochemistry and Physiology. Part C, Toxicology & Pharmacology*, **131**, 1-8.

57. Peiris OA, KDP. Wimalaratne, A. Nimalasuriya (1969). Exchange transfusion in the treatment of Russell's viper bite. *Post graduate Med. J.,* **45**: 627-629.

Annexure

ANNEXURE

PROFORMA

ANALYSIS OF ACUTE RENAL FAILURE IN POISON CONTROL AND TOXICOLOGY TRAINING CENTRE

1. Name
2. Age
3. Sex
4. IP NO
5. Date of Admission
6. Date of Discharge / Expiry
7. H/o type of Poison
8. H/o comorbid illness
9. Time of onset of Oligonuria

EVALUATION

1. Blood Pressure
2. Complete blood count

3. Peripheral smear

4. Blood Urea

5. Serum creatinine

6. Serum Lactate dehydrogenase

7. Serum alanine aminotransferase

8. Whole blood clotting time

9. Urine analysis

10. Ultrasonogram abdomen

11. Type of dialysis

12. Outcome

MASTER CHART

S. No	Name	Age	I.P. No.	DOA	DOD/ DOE	Etiology	Time of onset of oligoanuria	Predisposing factors	Urine Output	Urine Albumin	Urine RBC's	RFT at admn. Urea	Sr. Cr	Na+	K+	USG KUB	Time of start of specific treatment for etiology (Hrs)	Mode of treatment of ARF	Out come	RFT at discharge U/Sr.Cr.
1.	Elumalai	35	86123	26.12.06	01.01.07	Snake bite	18	Hemolysis	Oliguria	3+	+	109	5.4	124	5.6	↑Cortical echoes	36	HD	Expired	1
2.	Madhan	18	58	03.01.07	10.01.07	Scorpion sting	60	Myocarditis	Oliguria	Nil	Nil	54	1.9	129	3.7	"	24	Conser-vative	Improved	30/0.9
3.	Chengaiah	50	1281	06.01.07	15.02.07	Snake bite	48	No	Non Oliguria	3+	+	154	15.2	116	6.1	"	36	HD	ESRD	96/4.6
4.	Rajeeswari	30	3709	18.01.07	20.01.07	Dichromate	24	Hepatic failure	Oliguria	Nil	Nil	100	5.8	134	5.8	"	24	HD	Expired	1
5.	Kotteswaran	30	4752	22.01.07	03.02.07	Snake Bite	48	Hemolysis	Non Oliguria	Nil	Nil	68	3.9	120	3.4	"	18	Conser-vative	Improved	34/1.0
6.	Ravi	20	12579	23.02.07	13.03.07	Snake Bite	36	Hemolysis	Oliguria	2+	+	143	5	118	4.6	"	24	HD	Improved	38/1.2
7.	Kannaiyan	55	12826	25.02.07	15.03.07	Snake Bite	24	Nil	Oliguria	2+	+	98	2.4	126	5.4	"	36	HD	Improved	38/1.2
8.	Madhavan	42	13154	27.02.07	04.03.07	Snake Bite	36	Hemolysis DIC	Oliguria	2+	+++	90	5.3	122	4.8	"	24	HD	Expired	1
9.	Ethiraj	55	15025	06.03.07	13.03.07	Snake Bite	24	Hemolysis	Non Oliguria	+	+	70	2.4	128	3.9	"	24	Conser-vative	Improved	44/1.4
10.	Ramalingam	63	18871	22.02.07	11.04.07	Snake Bite	24	Hemolysis	Oliguria	3+	++	101	3.7	121	4.9	"	18	HD	Improved	40/1.3
11.	Annadurai	34	17238	16.03.07	06.04.07	Snake Bite	24	Hemolysis	Oliguria	2+	2+	90	2.8	125	4.5	"	12	HD	Improved	46/1.3
12.	Mariammal	37	21342	02.04.07	03.04.07	Snake Bite	36	Hemolysis	Oliguria	+	+	187	7.3	116	5.8	"	23	HD	Expired	1
13.	Murugan	30	20670	30.03.07	15.04.07	Snake Bite	18	No	Oliguria	3+	++	141	5.4	139	4.9	"	36	HD	Improved	40/1.1
14.	Amutha	14	84513	14.10.06	01.11.06	Snake Bite	36	Hemolysis	Oliguria	2+	+	118	5.0	128	3.5	"	24	HD	Improved	30/0.9
15.	Babu	35	25303	19.04.07	12.05.07	Snake Bite	36	Hemolysis	Oliguria	4+	+	160	3.3	133	5.8	"	24	HD	Improved	36/1.2
16.	Mani	30	28356	01.05.07	16.05.07	Indigenous medicine	48	No	Non Oliguria	Nil	Nil	110	6.0	142	5.7	"	–	HD	Improved	40/1.3
17.	Kesavalelu	40	29332	05.05.07	24.05.07	Snake Bite	36	No	Oliguria	2+	+	80	8.9	132	5.6	"	24	HD	Improved	36/1.1

S. No	Name	Age	I.P. No.	DOA	DOD/ DOE	Etiology	Time of onset of oligoanuria	Predisposing factors	Urine Output	Urine Albumin	Urine RBC's	RFT at admn. Urea	Sr. Cr	Na+	K+	USG KUB	Time of start of specific treatment for etiology (Hrs)	Mode of treatment of ARF	Out come	RFT at discharge U/Sr.Cr.
18.	Krishnan	31	31553	14.05.07	16.05.07	Rat Killer	72	Hepatic Failure	Oliguria	Nil	Nil	143	7.3	130	6.0	"	–	PD	Expired	1
19.	Raja	30	32873	15.05.07	20.05.07	snake bite	96	No	Oliguria	2+	+	170	2.0	134	4.9	"	36	Conser-vative	Improved	32/1.0
20.	Ravi	35	35058	28.05.07	01.06.07	Shell Oil	24	MODS	Non Oliguria	Nil	Nil	164	8.3	126	4.3	"	–	PD	Expired	1
21.	Munusamy	45	38207	09.06.07	28.06.07	Snake Bite	24	No	Oliguria	2+	+	121	3.3	126	5.9	"	24	HD	Improved	33/1.1
22.	Thimmaiyan	40	39558	16.06.07	10.07.07	Snake Bite	48	No	Oliguria	3+	+	223	18.7	130	3.9	"	24	HD	Improved	40/1.3
23.	Elumalai	40	43582	01.07.07	05.07.07	Snake Bite	36	No	Oliguria	+	Nil	65	2.4	130	4.2	"	18	Conser-vative	Improved	29/0.9
24.	Villisamy	42	43687	02.07.07	15.07.07	Snake Bite	72	Dehydration respiratory failure	Non Oliguria	Nil	Nil	100	2.3	132	3.3	"	12	Conser-vative	Expired	30/1.0
25.	Ramesh	34	48849	21.07.07	30.07.07	Snake Bite	36	No	Oliguria	2+	+	196	16	110	6.4	"	24	HD	Improved	32/1.1
26.	Shisaiyan	46	48554	20.07.07	15.08.07	Snake Bite	36	No	Oliguria	+	Nil	163	7.2	134	6.0	"	24	HD	Improved	36/1.2
27.	Mangalam	42	48790	20.07.07	22.07.07	$CuSO_4$	48	Hemolysis hepatic failure	Oliguria	Nil	+	183	6.4	130	6.2	"	24	PD	Expired	1
28.	Velu	34	47334	16.07.07	08.08.07	Snake Bite	96	No	Oliguria	Nil	Nil	187	7.8	142	5.2	"	48	HD	Improved	33/1.0
29.	Rajendran	52	55124	26.07.07	20.08.07	Wasp bite	96	No	Oliguria	Nil	Nil	224	13.4	132	6.4	"	–	HD	Improved	38/1.2
30.	Babu	40	2552	12.01.07	14.02.07	$CuSO_4$	48	Hemolysis hepatic failure	Oliguria	Nil	Nil	143	7.2	136	4.2	"	36	PD	Expired	1
31.	Bashrao	30	862630	29.12.06	30.12.06	Vasmol 33	24	Hepatic failure	Oliguria	Nil	Nil	164	6.3	124	6.4	"	–	PD	Expired	1
32.	Bakiyalakshi	26	838679	17.09.06	18.09.06	Rat killer	24	Hepatic failure	Oliguria	Nil	Nil	194	7.6	126	5.4	"	–	PD	Expired	1

INSTITUTIONAL ETHICAL COMMITTEE
Government General Hospital & Madras Medical College,
Chennai – 600 003, India.
Off. Ph. No. 044-25305000
Fax: 044-25305115

Ref. No.: 12299 / P&D / Ethics / Dean / GGH / Chennai, dated July 19th, 2007

Title of the Work: Analysis of acute renal failure in poison control and toxicology training centre

Principal Investigator: Dr. R. Sakthirajan

Department: Institute of Internal Medicine, MMC, Chennai

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on **July 19th 2007**, at the conference hall of the Dean, Tower Block I, GGH, Chennai.

The members of the committee, the secretary, and the chairman are pleased to
- approve the proposed work mentioned above, submitted by the principal investigator /
- ~~consider the proposed work but advised for revision and resubmission~~.

The principal investigator and their team are directed to adhere the guidelines given below:

01. You should get detailed informed consent from the patients / participants and maintain confidentiality.
02. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
03. You should inform the IEC in case of any change of study procedure, site and investigation or guide.
04. You should not deviate form the area of the work for which I applied for ethical clearance.
05. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
06. You should abide to the rules and regulations of the institutions(s).
07. You should complete the work within the specific period, and if any extension of time is required, you should apply for permission again and do the work.
08. You should submit the summary of the work to the ethical committee on completion of the work.
09. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.

Secretary,
IEC, GGH, Chennai.

Chairman,
IEC, GGH, Chennai.

Dean,
GGH & MMC, Chennai.